



ICAO

Doc 10152

Manual on Testing and Cross-border Risk Management Measures

First Edition, 2020



Approved by and published under the authority of the Secretary General

INTERNATIONAL CIVIL AVIATION ORGANIZATION



| ICAO

Doc 10152

Manual on Testing and Cross-border Risk Management Measures

First Edition, 2020

Approved by and published under the authority of the Secretary General

INTERNATIONAL CIVIL AVIATION ORGANIZATION

Published in separate English, Arabic, Chinese, French, Russian
and Spanish editions by the
INTERNATIONAL CIVIL AVIATION ORGANIZATION
999 Robert-Bourassa Boulevard, Montréal, Quebec, Canada H3C 5H7

For ordering information and for a complete listing of sales agents
and booksellers, please go to the ICAO website at www.icao.int

First edition, 2020

Doc 10152, *Manual on Testing and Cross-border Risk Management Measures*
Order Number: 10152
ISBN 978-92-9265-220-3

© ICAO 2020

All rights reserved. No part of this publication may be reproduced, stored in a
retrieval system or transmitted in any form or by any means, without prior
permission in writing from the International Civil Aviation Organization.

AMENDMENTS

Amendments are announced in the supplements to the *Products and Services Catalogue*; the Catalogue and its supplements are available on the ICAO website at www.icao.int. The space below is provided to keep a record of such amendments.

RECORD OF AMENDMENTS AND CORRIGENDA

[illegible][illegible]

FOREWORD

This manual has been prepared by aviation health experts led by the International Civil Aviation Organization (ICAO) with support from the United States Centers for Disease Control and Prevention (CDC), European Centre for Disease Prevention and Control (ECDC) and others, with contributions from the World Health Organization (WHO) as well as aviation medical and health experts from governments and industry. Together they form the Collaborative Arrangement for the Prevention and Management of Public Health Events in Civil Aviation (CAPSCA). CAPSCA brings together international, regional, national and local organizations to work together to improve preparedness planning and response to public health events that affect the aviation sector.

CAPSCA developed this guidance in close collaboration with the ICAO Council Aviation Recovery Task Force (CART), which requested updated guidance on the inclusion of COVID-19 testing and its interdependencies with other risk mitigation tools for those States that choose to include testing as an element of their overall COVID-19 risk management process.

The CART has published updated recommendations to States in the High-Level Cover Document (HLCD) including Recommendation 13 on testing: "While testing is not universally recommended by public health authorities as a routine health screening method, States contemplating testing in their COVID-19 risk management strategy should apply the approach outlined in the ICAO *Testing and Cross-Border Risk Management Measures Manual*".

Updates to the CART Take-off Guidance for Air Travel through the COVID-19 Public Health Crisis (TOGD) focus on the evolving technological and medical advancements in the fight against COVID-19 and providing targeted guidance to effectively support States in their efforts to control the pandemic while pursuing the restart and recovery of aviation. In this regard, specific attention is being brought to testing as a potential means to alleviate quarantine measures and thus facilitate international movement of people and goods, as part of a multilayer risk management strategy.

This guidance supplements the measures already outlined in the CART HLCD and TOGD and provides a risk management process to facilitate States' assessment of the applicability of a combination of measures available today.

COVID-19 testing, if applied according to the guidance contained in this manual, could reduce reliance on measures that restrict air travel and the movement of persons arriving in a country, such as quarantine, which evidence suggests is a disincentive to several important categories of travel of which the following list is non-exhaustive: pilot certification, pilot simulator training, essential business flights and tourism for some States which are dependent on inbound tourism for economic sustainability.

In implementing testing as a component of their overall COVID-19 risk management strategy, States are advised that an effective application of a multi-layered risk strategy, including testing, is one in which:

- a) States perform a risk assessment using epidemiologic criteria including but not limited to disease prevalence, disease trajectory, national testing strategy, screening capabilities, hospital capacity and robustness of contact tracing;
- b) States share the results of the risk assessments, the local epidemiology and transmission scenarios in the departure and destination countries or areas as well as the public health and health system capacity and performance to detect and care for returning travellers and their contacts; with other States to facilitate the opening of air routes;
- c) States consider their risk tolerance as a part of their risk assessment;

- d) States use their risk assessment and risk tolerance in determining the application of a multi-layered risk management strategy;
- e) States that select to utilize testing for screening purposes apply a cut-off value for sensitivity and specificity as high as possible (with a minimum of 95 per cent) to reduce false positive test results;
- f) States, when addressing higher risk scenarios and applying testing as part of the multi-layer risk management strategy, take into account the test result when considering the need for and duration of isolation or quarantine; and
- g) States harmonize their procedures to the extent possible.

This manual describes the risk management measures which can be applied; how epidemiology can be used to advise States in developing a risk management strategy; possible testing protocols which might be put in place where there is differential prevalence, and therefore risk; and a series of examples to help States in their decision-making process.

TABLE OF CONTENTS

	<i>Page</i>
Glossary	(ix)
Chapter 1. Introduction	1-1
Chapter 2. General risk management principles applied to air transport	2-1
Chapter 3. Testing and cross-border risk management measures.....	3-1
3.1 Overview	3-1
3.2 Assessment of epidemiological indicators	3-2
3.3 Testing as a screening strategy applied to aviation	3-3
3.4 Quarantine practices	3-6
3.5 Combined testing and quarantine strategies	3-7
Chapter 4. Implementation — Combined strategies.....	4-1
4.1 Overview	4-1
4.2 Possible model for risk assessment and determining mitigation measures (four-step process).....	4-2
4.3 Sample scenarios	4-6
Attachment A. Decision aid	Att A-1
Attachment B. Epidemiologic primer	Att B-1

GLOSSARY

LIST OF ACRONYMS

API	Advance Passenger Information
CAPSCA	Collaborative Arrangement for the Prevention and Management of Public Health Events in Civil Aviation
CART	Council Aviation Recovery Task Force
ECDC	European Centre for Disease Prevention and Control
HLCD	High-Level Cover Document
ICAO	International Civil Aviation Organization
IHR	International Health Regulations
NPV	Negative predictive value
PCR	Polymerase chain reaction
PHC	Public Health Corridor
PNR	Passenger Name Record
PPE	Personal protective equipment
PPV	Positive predictive value
RT-PCR	Reverse-transcription polymerase chain reaction
TOGD	Take-off Guidance for Air Travel through the COVID-19 Public Health Crisis
WHO	World Health Organization

DEFINITIONS

Epidemiology. The branch of medicine which deals with the incidence, distribution and possible control of diseases and other factors related to health.

False negative test. A result that indicates that the disease is not present when the person actually does have the disease.

False positive test. A result that indicates that the disease is present when the person actually does not have the disease.

Incidence. The number of new cases in a specified population during a specified period of time.

Negative predictive value (NPV). How likely a negative test is a true negative.

Positive predictive value (PPV). How likely a positive test is a true positive.

Prevalence. Disease burden expressed as a percentage or rate with the total population as the denominator; in this context, the number of existing cases in a defined population at a given point in time.

Sensitivity. The likelihood that a test will correctly identify a person with the disease; the “true positive” rate.

Specificity. The likelihood that a test will correctly identify a person without the disease; the “true negative” rate.

Chapter 1

INTRODUCTION

1.1 This guidance is intended for use by State regulators, service providers and other concerned entities, and it addresses cross-border risk management in commercial air transport operations. The objective of the guidance is to inform States about public health risk management strategies to reduce the probability of translocation of the disease from one region to another. Updates will be provided as new scientific evidence becomes available. This document contains guidance for implementing a systemic process to identify risks related to the COVID-19 pandemic and mitigate those risks to an acceptable level as determined by each individual State. The final objective is to create a harmonized and cooperative effort to maintain global connectivity.

1.2 The guidance provides assessment tools that States can use to evaluate and implement measures as part of their decision-making process. For this purpose, an example of the process is presented and applied to a strategy that utilizes a range of risk mitigation measures. This guidance does not constitute a recommendation for application of any specific measure but rather a guideline on how to assess different mitigation strategies and on how they can contribute to public health risk management. As an example of this approach, the document will provide the description of a strategy based on the assessment of epidemiological indicators, testing and quarantine practices. Additional detailed guidance for States will be included as annexes by ICAO and the WHO.

1.3 This manual has been developed using the most recent information as of its publication date. The urgency, rapid development, and observed consequences of the current scenario required an expedited approach based on expert consensus and current scientific evidence. Consequently, regular updates will be required as the evidence evolves and as technology advances. Data-driven adjustments to the guidance will be made as the situation evolves.

1.4 Each State will need to conduct its own assessment and is encouraged to use the processes outlined in this manual as the basis for its assessment. Risk tolerance varies between States and depends on many factors. This has an influence on the amount of residual risk a State can accept. The determination of such level cannot be universal as it depends on specific priorities and the sovereignty of each individual State.

Chapter 2

GENERAL RISK MANAGEMENT PRINCIPLES APPLIED TO AIR TRANSPORT

2.1 The principles of a “generic risk management process” are considered appropriate in the context of a public health risk management framework. The objective of this process is to identify the residual risk, taking into consideration existing risk mitigation measures, of transporting an infectious passenger or translocating COVID-19 from one State to another.

2.2 To support States in developing a risk assessment framework that is adapted to sovereign considerations and integrates with existing national frameworks, ICAO developed a generic decision-making tool (see Attachment A). The tool can be used to determine the inherent and residual risk level of transporting potentially infectious passengers.

2.3 The proposed risk assessment process relies on a circular process that considers risk holistically by defining a risk scenario instead of focusing on a single hazard or threat. The determination of an inherent risk results from evaluating the likelihood of the risk scenario, as well as defining the resulting impact. It is essential to consider risk management measures which are already in place when conducting the initial assessment of the inherent risk. This step of the risk assessment process cannot consider future or potential management measures as it intends to provide the “as is” situational assessment. The result provides States with information relevant to determining if the risk scenario lies within its public health management capacity. As the inherent risk changes, States will need to modify their risk management measures. In addition, States should consult the *Safety Management Manual* (Doc 9859) and the *ICAO Handbook for CAAs on the Management of Aviation Safety Risks related to COVID-19* (Doc 10144).

2.4 The modelling of a risk scenario is the starting point in the use of the tool, based upon the existing situational assessment but considering multi-sector collaboration within the context of the State. A generic baseline example for such a scenario could be “the risk to be assessed is of an infectious person being on board an international flight” or “the risk of translocation of the virus through air transport”. The shape of the risk scenario will need to address a State’s view on what it considers as the most critical aspect of public health management. The tool then progresses through different available management solutions that affect the risk’s likelihood and impact, as defined in Box 1. It is designed in a way that the efficacy of each management measure can be qualitative.

Box 1. Risk management terminology

Risk avoidance. It is often the most powerful tool of risk management and aims at reducing the likelihood of risk by avoiding it. It is, however, also the most limiting tool in terms of environmental continuity.

Risk mitigation. It aims at reducing the impact of the risk (by addressing the likelihood, magnitude, or both when risk cannot be avoided).

Risk transfer. It aims to move the impact of the risk to a different environment. This is complex and should only be used if the risk can be fully measured, addressed and mitigated by the environment it is transferred to (an example could be to transfer risk to a State with better health care capacity).

Risk acceptance. It is the process of accepting the consequence (impact) of a risk. This technique is often advisable only when the risk is small but may need to be considered in complex risk scenarios.

2.5 Risk mitigation appears to be the most appropriate strategy in the context of pandemic risk management in air transport. In the further conduct of the risk assessment process, it will be necessary to choose from all available and fast-evolving mitigation measures such as requiring masks, passenger locator forms, testing, physical distancing, etc., at airports and during flights. There may be limited scientific peer-reviewed evidence-based efficacy for these mitigation measures, and the scope of their impact on transforming the inherent risk is based on expert consensus and existing available evidence. As a result, much of the risk assessment is qualitative and, as such, provides the elasticity to be adopted and integrated into existing national public health and aviation plans. The risk assessment process will consider the chosen mitigation measures, and by re-evaluating how they affect the likelihood and impact of the inherent risk. A State can then determine if the residual risk is within public health management capacity.

2.6 The tool's crucial conclusion is that the determination of the residual risk is within the public health management capacity of the State concerned. This determination needs to be done under the sovereignty and responsibility of each State. Faced with a fast-evolving pandemic, the risk assessment process must be regularly repeated if a State is to be confident that its mitigation measures are keeping the risks within the capacity of its public health system.

Chapter 3

TESTING AND CROSS-BORDER RISK MANAGEMENT MEASURES

3.1 OVERVIEW

3.1.1 Air connectivity will be essential to enable economic recovery. As States endeavour to restart international travel, they will need effective strategies for mitigating the risk of active case importation and disease transmission within the air transport system. Mitigation strategies include transmission suppression and control, testing, and other tools such as symptom screening. States will rely on community accountability and ownership, traveller education, and other collaborative cross-border measures in accordance with international recommendations from health authorities.

3.1.2 Given the high complexity of the current public health crisis, there is no single measure that can be deemed as a definitive solution. Every mitigation measure affects the system in different ways. States should identify and compare levels of risks cognizant that public health risks cannot be eliminated. The following guidelines are meant to assist States in understanding how current mitigation measures can contribute to managing public health risks.

3.1.3 Emerging strategies should be considered and revised as new scientific evidence is published, innovative approaches are tested, and potential outcomes are modelled. As the pandemic dynamics evolve, new approaches such as probabilistic models, innovative testing technologies, air quality improvement, disinfection methods, immunizations and other processes are under rapid development and should be added to the strategies as their efficacy and cost-effectiveness is substantiated.

3.1.4 Throughout this chapter, it is assumed that the recommended protective layers have been considered in the formation of Public Health Corridors (PHCs) in accordance with the CART TOGD and the CART HLCD Recommendation 14: “States considering the formation of a Public Health Corridor (PHC) should actively share information with each other to implement PHCs in a harmonized manner. To facilitate implementation of PHCs, the ICAO Implementation Package (iPack) on establishing a PHC is available to States”.

3.1.5 The layered defence measures against COVID-19 include the steps being taken at airports and on board and is described in more detail in the iPack. It may include some or all of the measures listed below:

- a) temperature testing and/or asking about symptoms (fever, loss of sense of smell or taste, chills, cough, shortness of breath, etc.);
- b) self-awareness orientation to allow passengers to identify symptoms and complete/submit health declarations or health attestations;
- c) enhanced cleaning and disinfection; contactless boarding/baggage processing; use of physical barriers and sanitization in airports;
- d) physical distancing in airports and during boarding; use of face coverings or masks; separation between passengers on board when feasible;

- e) adjustment of food and beverage service to reduce contact; control of access to aisles and bathrooms to minimize contact;
- f) limiting exposure of crew members to infection; and
- g) facilitation of contact tracing in the event that a passenger develops infection.

3.2 ASSESSMENT OF EPIDEMIOLOGICAL INDICATORS

3.2.1 States could consider implementing testing as part of their COVID-19 risk management strategy, taking into consideration the principles of a “generic risk management process” (Chapter 2 and Attachment A) and the detailed epidemiology primer (Attachment B).

3.2.2 A critical step in assessing risk for States is understanding the real time epidemiologic indicators of prevalence and the disease trajectory (escalated spread or diminishing cases) in addition to the availability of testing, health care system saturation, and robustness of contact tracing. Studying these factors will allow countries to compare disease rates between points of origin and arrival by member States or region, and in some cases by cities depending on the detail of the disease reported by public health authorities and the ability of a State or region to correctly identify and treat ill people. There are several sites reporting rolling averages of new cases per 100 000 people including the WHO (<https://covid19.who.int/>), the ECDC (<https://gap.ecdc.europa.eu/public/extensions/COVID-19/COVID-19.html#global-overview-tab>) and Brown School of Public Health (<https://globalepidemics.org/key-metrics-for-covid-suppression/>). The reliability of the case numbers is affected by the availability of tests, testing intensity, and the national testing strategy in each phase of the pandemic.

3.2.3 Prevalence is the proportion of the population with a disease at a given time. In considering the goal of lowering the risk of disease transmission during travel and disease translocation risk to the destination country, the potential number of persons on board an aircraft who could be infectious during the travel experience is vital. That data must be inferred as there is no current ability to determine it directly through routine surveillance testing. It can be estimated by multiplying the cases per 100 000 by the infectivity period and then factoring in the asymptomatic rate. This number is then converted to a percent infectious per 100 persons. In this case, prevalence is a better indicator of potentially infectious individuals than incidence (new cases per day); however, an awareness of incidence will influence the shrinking or growth of the disease cases in a given area.

3.2.4 Disease trajectory refers to whether the number of new cases of disease remains stable, increases or decreases over time. An awareness of which way the infection rates are going may assist in monitoring risk. For instance, if a State level of disease is in a moderate range, but there is a doubling of case rates per week, a State may want to rethink requirements or risk mitigation strategy.

3.2.5 To gain a true picture of the prevalence and trajectory of disease, testing should be readily available and utilized routinely when individuals are either displaying symptoms or are identified as close contacts. States may wish to consider the proportion of testing compared to the population, the percentage of positive results, and the proportion of positive tests in symptomatic or close contacts compared to asymptomatic persons. Testing strategy is further detailed in WHO's interim guidance on laboratory testing (https://apps.who.int/iris/bitstream/handle/10665/331509/WHO-COVID-19-lab_testing-2020.1-eng.pdf?sequence=1&isAllowed=y).

3.2.6 States can use this information to classify or stratify cities, States, or regions by risk level (see Chapter 4). By developing these benchmarks, States and regions can begin to discuss mitigation strategies necessary between States.

3.3 TESTING AS A SCREENING STRATEGY APPLIED TO AVIATION

3.3.1 Testing concepts

3.3.1.1 While testing is not universally recommended by public health authorities as a routine screening method for asymptomatic international travellers, it has been implemented by some States for this purpose. For those States desiring to employ testing as a part of an overall risk mitigation strategy, the following concepts should be considered:

- a) Reducing risk to zero is impossible, but testing can be one measure in the risk mitigation system.
- b) There are three reasons to consider testing:
 - 1) reducing transmission during the actual travel;
 - 2) reducing potential introduction of disease in a region/country, and
 - 3) potentially reducing or eliminating quarantine for the traveller at their destination.
- c) States should consider including the concept of limiting the exportation of disease and developing methods to communicate to travellers the need to remain at their residence when ill, when in isolation, when in quarantine, if they have a pending test following the onset of symptoms compatible with COVID-19 and any other relevant measures as recommended by the relevant Public Health Authority.
- d) The current approved COVID-19 tests that are recommended by public health authorities are for testing of symptomatic or exposed individuals for diagnostic purposes. Use in an asymptomatic population may yield different test performance than that of symptomatic cases. In Attachment B, Epidemiologic primer, a margin of error is described and used to account for asymptomatic cases in the development of the positive and negative predictive values.
- e) In areas with low test availability, States should balance the diagnostic needs in symptomatic individuals and individuals related to high risk settings against screening of healthy or asymptomatic potential travellers.
- f) Testing should be performed by individuals trained to perform the test at a site approved by the appropriate authorities. The test outcome should be a confirmed test result that the traveller can present to authorities. Test results presented for traveling purposes must be verified if there is any uncertainty as to the validity of the result. It is foreseen that a standardised form to report tests results will be developed in the future to facilitate recognition by different authorities as part of the PHC approach.

3.3.2 Testing methods and performance-based recommendation

3.3.2.1 At the time of publication, molecular testing (e.g. real-time RT-PCR) is recommended by the WHO for routine diagnosis, some rapid antigen tests have been recommended for emergency use but not as a diagnostic test for points of entry¹; while serological tests are not considered suitable for diagnosis of an active COVID-19 infection.

1. <https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays>

3.3.2.2 As more and different tests are approved for emergency use, including some that were previously considered to be less effective, specifying a particular test or set of tests as the “best” regimen to use becomes challenging. Each of these tests has distinctive advantages and disadvantages which need to be considered.

3.3.2.3 One of the aims of this guidance is to establish a performance-based recommendation for testing regardless of the methodology that the States could consider if using testing as a part of their risk mitigation measures. This is aligned with the ICAO risk-based approach, supporting State sovereignty to make decisions based on a State’s risk assessment and risk tolerance, guided by their own priorities and consideration of epidemiological indicators, practical testing limitations and other relevant considerations.

3.3.2.4 States are advised to:

- a) consider the performance of the test being considered for use;
- b) implement a strategy to manage positive and false positive test results, e.g. confirmatory testing;
- c) record and review testing data on a frequent basis;
- d) monitor scientific developments; and
- e) adjust their testing protocols accordingly.

3.3.3 Pre-departure screening

The goal of pre-departure testing is to limit the potential transmission of COVID-19 during travel and may contribute to the reduction in the risk of translocation of the disease. Pre-departure testing can reduce in-flight transmission by up to 75 per cent. No testing regimen can reduce the risk to zero; hence, travellers must continue to employ routine recommended public health measures. The current understanding of COVID-19 allows the assumptions below. The closer the testing is to departure, the more likely the person will remain unable to infect others during the journey. Testing too far in advance of departure results reduces the advantage of the risk reduction allowed by pre-departure screening. The optimum risk reduction results can be achieved by testing within 48 hours of departure. This conclusion is based upon the following:

- a) incubation time: 2 to 12 days (95 per cent of cases) with a median of 5 to 6 days;
- b) viral shedding can occur 48 hours prior to symptom onset;
- c) the most sensitive tests turn positive 1 to 3 days (24 to 72 hours) prior to symptoms; and
- d) leaving a 2- to 4-day period where a person could be infected but not contagious while travelling (i.e. a negative test if the median incubation period is used). However, this could miss very short incubation cases.

3.3.4 Post-arrival screening

Post-arrival screening, in conjunction with pre-departure testing, can result in risk reductions. Consequently, as part of a State’s risk assessment and determination of risk tolerance, it may consider reducing quarantine time frames. Additional modelling and close follow up of travellers will further refine when to test moving forward. Refer to the tables and references in Chapter 4, 4.2 for more detailed information.

3.3.5 Combined pre-departure and post-arrival screening

Modelling suggests that pre-departure screening, preferably close to departure, in combination with post-arrival testing on day 4 to 5 and a shorter quarantine, may perform as well as a 14-day quarantine alone. These models are currently undergoing further refinement, and updated findings will be included in future revisions.

3.3.6 Selecting test devices based on statistical analysis

Note.— See Attachment B, Epidemiologic primer for definitions and sample equations.

- With the goal of allowing the greatest number of people to travel, the test device in the prevalence level in the traveller's population should have a high negative predictive value, meaning a negative test is in all likelihood truly negative. While there will be a few false negatives who would enter the system, the bigger issue will be a significant number of false positives who are not infected and could travel otherwise. A plan to evaluate the false positives should be developed.
- Even tests with relatively low specificity (the ability to correctly identify those who do not have the disease as negative), result in high negative predictive values. Establishing a higher test sensitivity cut-off (i.e. the ability to correctly identify those with the disease) will limit those with the disease but who might enter the travel corridor or be released from quarantine.
- For those States choosing to utilize testing, it is recommended that the cut-off values for sensitivity and specificity be as high as possible, but with a minimum of 95 per cent² (sensitivity cut-offs are based on reported sensitivity for cases in the peak contagious period, not for very early or very late stage infections). Given the reported test values were from the manufacturers as part of their Emergency Use Agreement applications, where possible independently validated sensitivities and specificities should be used. No specific diagnostic test(s) is recommended as the number of fielded test devices are growing too rapidly. Hence, a performance-based approach to the selection of a test device(s) using sensitivity and specificity is preferred.
- Polymerase chain reaction (PCR) tests are in short supply in some States and typically expensive. Due to short supply, PCR tests are often reserved only for symptomatic individuals. This might cause significant delays in obtaining results. They are usually based on swab techniques which require suitable trained personnel, premises, and equipment for the sampling process. This means they are difficult to apply in an airport setting. Many countries are calling for pre-travel PCR tests, but this creates problems of a window of possible infection after testing, as well as requirements for test approval, identity verification and fraud-proofing of the test results. These have led to interest in using more rapid point-of-care tests including antigen tests that could be used for screening purposes, with consideration of protocols to manage positive test results.

2. The recommendation for a minimum sensitivity and specificity level of 95 per cent is based on the following:

- The minimum values of 95 per cent for sensitivity and specificity will allow for a wider range of test devices to be used that are currently fielded as opposed to forcing States to procure newer models that are frequently hard to obtain.
- This range also allows for the use of rapid antigen tests as a screening device which are more accessible and practical for application in the aviation environment; and are faster and less expensive to use. In addition, it would reserve the more expensive real-time RT-PCR tests for confirmation of positives in conjunction with clinical correlation.
- Setting the specificity at 95 per cent maintains a high NPV and reduces the false positives.
- Setting the sensitivity at 95 per cent will also reduce the risk of false negatives and improve the PPV.
- In low prevalence settings (equating from 10 to 25 cases per 100 000 on a rolling average), the NPV equates to mislabelling an infected person as negative between 1 in 5 000 and 10 000 negative tests. In a higher prevalence setting (equating to over 50 cases per 100 000 on rolling average) the mislabelling rises close to 1 in 300.
- In the same low prevalence and higher prevalence range, the PPV improves from correctly labelling of positive from approximately 5 to 10 per cent, to slightly better than 1 out of 2 of positive tests.
- These are minimum recommended values. States should determine their own minimum levels for sensitivity and specificity that they may require to improve test performance.

3.3.7 Management of positive tests

All positive tests should be referred for clinical correlation to reconfirm the diagnosis and isolation requirements. Test results should be interpreted in the context of the prevalence of infection or disease, the device's performance characteristics and instructions for use, as well as the patient's clinical signs, symptoms and history. For positive rapid antigen tests in particular, a confirmative test can be considered when the pre-test probability is low, such as asymptomatic individuals with no known exposure.

3.4 QUARANTINE PRACTICES

3.4.1 Many States have instituted a period of quarantine for incoming passengers as a measure to prevent importation of new cases. According to the International Health Regulations (IHR), quarantine means "the restriction of activities and/or separation from others of suspect persons who are not ill [...] in such a manner as to prevent the possible spread of infection or contamination". Isolation means "separation of ill or contaminated persons [...] in such a manner as to prevent the spread of infection or contamination". WHO defines a "contact" as "a person in any of the following situations from two days before and up to fourteen days after the onset of symptoms in the confirmed or probable case of COVID-19: face-to-face contact with a probable or confirmed case of COVID-19 within one meter and for more than fifteen minutes, direct physical contact with a probable or confirmed case of COVID-19, direct care for an individual with probable or confirmed COVID-19 without using proper personal protective equipment; or other situations, as indicated by local risk assessments." States' implementation of quarantine measures varies and may range from voluntary self-quarantine, to quarantine in their residence and to enforced restrictions at specified locations.

3.4.2 The quarantine period tends to be 14 days to exceed the usual maximum incubation period. There can be considerable logistical difficulties and cost in implementing a quarantine regime, and States electing to utilize quarantine need to plan and prepare accordingly. Depending on the implementation model, States may need to ensure that all needs for transport, accommodation, food, exercise and communication are met, in line with the IHR, and that there is no cross-contamination between those in the quarantine facility including the staff. In some cases, given the frequency of asymptomatic infection, the quarantine is now accompanied by COVID-19 testing. With the addition of testing effectiveness of a quarantine regime in preventing the entry of infected travellers is increased as it is not solely dependent on people recognizing and reporting symptoms.

3.4.3 The WHO identifies scenarios in which quarantine could be implemented³. In accordance with WHO guidance, contacts of confirmed cases should be quarantined or asked to self-quarantine as part of national response strategy. For travellers, the WHO recommends self-monitoring for symptoms on arrival for 14 days, report symptoms to local authorities and follow national protocols. If States choose to implement quarantine measures for all passengers upon arrival, they should do so based upon a risk assessment and consideration of local circumstances. While quarantine can be an effective means of ensuring any imported cases by asymptomatic passengers do not spread the disease in the community, it can be a disincentive⁴ to travel, particularly if required after both (outbound and return) legs of an international journey, as can government advisories recommending against travel. Given the complexities and implications of quarantine, States choosing to implement a quarantine regime should do so after assessing all the implications, including non-health related implications, and considering them in accordance with their own national decision-making processes.

3. "Considerations for quarantine of contact of COVID-19 cases", Interim Guidance, WHO — 19 August 2020.

4. <https://www.iata.org/en/iata-repository/publications/economic-reports/travel-impact-of-quarantine2/>

3.5 COMBINED TESTING AND QUARANTINE STRATEGIES

3.5.1 For States that choose to apply quarantine measures, such measures should be implemented in conjunction with other public health interventions and in accordance with a risk-based analysis conducted by the destination State, considering the epidemiological situation of both origin and destination country or countries and other possible mitigation measures (see Section 3.2 above). A metric may be chosen to assist in this assessment, such as the test positivity rate.

3.5.2 In applying the risk assessment, States should consider their risk tolerance and the risks posed by the travel, and how different mitigation measures may reduce that risk. If travel is from an area of low prevalence to one of high prevalence, then the value of quarantine as a measure may be diminished. In situations where travel is between two countries with similar levels of transmission in the community, any travellers who had been tested negative for COVID-19, meeting the performance based criteria described in Section 3.3.2, upon departure would be of lower statistical risk than the non-tested members of the surrounding communities in either country. Travellers that have been tested negative for COVID-19 could be subjected to no more restrictions than the others in the community at destination.

3.5.3 While quarantine can have the highest impact when travel is from an area of high community transmission to an area of low community transmission, the introduction of testing into the measures applied could potentially be used to reduce the risk of translocation and the duration of quarantine. There is evidence to show that tests reduce the risk of an undetected positive case by some degree, and that a second test (in combination with a period of quarantine) further reduces that risk⁵.

3.5.4 On a careful analysis of the risks and evidence, as well as the government's risk tolerance, if the prevalence of infection at the point of origin of the passenger is less than (or equal to depending on risk tolerance) to the local prevalence at destination, and the passenger is not ill and/or has a negative test for COVID-19, governments might consider relaxing or avoiding quarantine measures. Alternatively, governments may determine that quarantine measures can be combined with other measures including testing to reduce the duration of quarantine.

5. Animal and Plant Health Agency (APHA), UK. Rachel A. Taylor, et al.; Tropical Medicine, UK, Samuel Clifford, et al and "Investigation into the effectiveness of "double testing" travellers incoming to the UK for signs of COVID-19 infection", Public Health England Modelling Cell.

Chapter 4

IMPLEMENTATION — COMBINED STRATEGIES

4.1 OVERVIEW

4.1.1 Many States have implemented risk mitigation strategies such as temperature measurements, traveller symptom questionnaires, COVID-19 testing, and a variety of travel restrictions such as border closures, entry bans from specific States, etc. However, these measures are not harmonized across States. Furthermore, there is very limited mutual recognition of mitigation measures even for States with equal prevalence. States should assess their own level of COVID-19 disease burden, health system capacity, availability of testing, and level of risk tolerance. Once established, States can share risk assessments with other States and begin to discuss developing bilateral agreements to open public health corridors and stimulate the return of air travel. Harmonization of procedures is crucial for facilitating air transport, and new practices should be coordinated with other States and stakeholders. In developing bilateral arrangements, States will need to consider the implications of hub traffic flows, and how they will accommodate third country-originating passengers.

4.1.2 To establish an internal State risk level, States should identify experts from State authorities, including but not limited to aviation (national authorities and industry), public health, customs and immigration, diplomatic organizations and legal departments, who can work collaboratively to assess the State's current status with respect to disease patterns. This collaborative assessment effort can be undertaken by each State's National Air Transport Facilitation Committee (or equivalent) as per CART report Recommendation 6, which urges Member States that have not done so, to immediately establish a National Air Transport Facilitation Committee as required by Annex 9 — *Facilitation*, in order to increase national level cross-sectoral coordination. The assessment should address the current capabilities to identify, diagnose, and treat COVID cases as well as the status of the health care system and the State's overall willingness and readiness to accommodate increased passenger flows. After reviewing this document and the CART Take-off guidance available on the ICAO public site (<https://www.icao.int/covid/cart/Pages/CART-Take-off.aspx>), States should identify the risk tolerance they can accept on a bilateral basis and the mitigation measures that could be employed to meet that target using a safety management system (SMS) approach.

4.1.3 Although data-driven decision making is encouraged, the current scenario may require a qualitative approach, as validated data and information is incomplete. By implementing a combined strategy and assessing if an acceptable residual risk is achieved, States should also evaluate alternatives to reduce or eliminate the burden to the system posed by selected mitigation measures. Some consideration must be given to how those measures should vary according to different stages of the pandemic (CART stages).

4.1.4 Procedures related to each phase and measure should be aligned and consider efficacy, costs and implementation challenges for each State.

4.1.5 Consistency with the State's national COVID-19 response policy and strategy is important, for example, medical masks may be recommended in aviation, but their availability should be prioritized for health workers and the public health response. In considering restrictions on aviation, the State should consider the role that aviation plays in the economy of the State and the public health response itself (such as the distribution of personal protective equipment (PPE), test kits, medicines and vaccines). States should ensure alignment between the various public policies and measures applied across government.

4.2 POSSIBLE MODEL FOR RISK ASSESSMENT AND DETERMINING MITIGATION MEASURES (FOUR-STEP PROCESS)

4.2.1 Introduction

This model has been developed to illustrate an approach that States could use on a bilateral or multilateral basis to assess risk at the points of origin and destination, and to assist in the selection of possible risk mitigation measures. States should tailor the process to suit their own national decision-making processes and conditions.

4.2.2 Step one — Determine that the following conditions have been met

This model is based upon the following assumptions (refer to CART Take-off guidance):

- a) travellers follow appropriate universal precautions at every stage of the travel continuum and:
 - 1) do not travel when sick;
 - 2) adhere to hand and respiratory hygiene practices;
 - 3) use a face covering/face mask (with exceptions as appropriate);
 - 4) practice physical distancing to the extent possible to lower the risk of disease spread; and
 - 5) adhere to instructions provided by airport and airline personnel;
- b) persons who test positive or are diagnosed with COVID-19 pre-travel do not travel and public health authorities are notified;
- c) persons who test positive at arrival isolate, and public health authorities are notified;
- d) close contacts of persons who test positive or are diagnosed pre-travel should be identified, quarantined, and not travel;
- e) close contacts of persons who are positive post travel should be identified (including fellow passengers), and quarantined. Where necessary, international contact tracing operations should be launched; and
- f) mechanisms are established to obtain and share complete, accurate and timely contact information to allow public health authorities to execute necessary public health actions.

4.2.3 Step two — Identify the effectiveness of existing measures

The table below lists a range of measures to reduce translocation of disease, estimated “effectiveness” of each measure and their implementation costs. Effectiveness in this context is defined as the extent to which the measure is estimated to reduce the risk of introducing infectious individuals into the community at the destination. The implementation costs depicted do not consider the impact of the measure on States’ economies.

<i>Mitigation strategy</i>	<i>Estimated effectiveness*</i>	<i>Implementation cost**</i>
Universal travel bans	Very high (100%)	Low
Selected travel bans	Varies depending on the State selection and the timing of the measure	Varies
Travel restrictions, do not board lists, for persons ill with COVID-19 or high-risk contacts who defy public health recommendations	High	Varies
<i>Pre-departure strategies:</i>		
Isolation of potential COVID-19 infected cases and quarantine of contacts	High	Varies
Single pre-departure testing	Low for preventing translocation*	Medium to low
Health declaration forms (symptom and contact checks)	Very Low	Low
Temperature screening	Very Low	Low
High ventilation	Medium	Low to medium
<i>In-travel strategies:</i>		
Traveller health education	Medium	Low
Using appropriate public health countermeasures	Medium	Low
Managing and positioning of sick passengers	Medium	Low
Reduce plane capacity	Low	Medium to high
Airflow and HEPA filters	Medium	Low

By comparison, pre-departure tests have a higher effectiveness mitigating transmission during the journey. With regards to preventing translocation, effectiveness increases the closer to the time of departure the test is carried out.

<i>Post-arrival strategies</i>		
Quarantine for 14 days upon arrival	High to very high (78-99% for State supervised quarantine)	Varies (State supervised quarantine can be high)
Data collection/sharing for proper contact tracing	Medium	Low
Single PCR testing	Medium (40%)	Medium
Health declaration forms (symptom and contact checks)	Low	Low
Temperature screening	Low	Low

<i>Combined testing/quarantine strategies</i>		
7-day quarantine followed by testing	Very high (94%)	High
5-day quarantine followed by testing	High (88%)	Medium
Post-arrival testing and 4-day quarantine followed by the second testing	Medium (69%)	Medium
4-day quarantine followed by testing	Medium (64%)	Medium
Pre-departure testing with post-arrival quarantine and testing	Currently being explored. Early models show similar rates to quarantine	Medium

* *The effectiveness estimates are based on:*

- a) *"Strategies to reduce the risk of SARS-CoV-2 re-introduction from international travellers", Samuel Clifford et al., Centre for Mathematical Modelling of Infectious Diseases, Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, UK;*
- b) *"The risk of introducing SARS-CoV-2 to the UK via international travel in August 2020", Rachel A. Taylor et al., Department of Epidemiological Sciences, Animal and Plant Health Agency (APHA), UK; and*
- c) *Public health authorities and expert consensus.*

** *Cost reflects the relative administrative expense of implementing a measure and is not meant to reflect societal or industry cost. States should consider the value of implementing a strategy with respect to potential gains of increased traffic. Note that these costs do not consider the impact of the measures on States' economies.*

4.2.4 Step three — Determine relative risks

The risk of translocating COVID-19 from one State to another can be determined by looking at three conditions within States: prevalence, test positivity rate and testing rate. The cut-off values associated with each condition below is intended to provide guidance on a possible framework for determining the risk levels in accordance with a colour code:

Potential cut-off values:

1. Prevalence — 7-day cases per 100 000 rate (rolling rate averages) with a cut-off of 25 cases per 100 000.

Note.— Some States favour using a rolling rate determined over a 14-day period.

2. Test positivity rate — 5 per cent as the cut-off with the goal of being below 5 per cent where tests are widely available for screening.
3. Testing rate — This condition would only be met if a State meets a testing capability of 250 tests per 100 000 people per week.

Possible colour coding based on conditions and cut-off values:

- Green: The origin State/area is below the cut-off values of 1 and 2 above.
- Orange: The origin State/area is below the cut-off value of 1 or 2 above, but not both.
- Red: The origin State/area exceeds the cut-off values of 1 and 2 above.
- Grey: there is insufficient data, or the State/area does not meet item 3.

4.2.5 Step four — Determine measures based upon identified risk levels

4.2.5.1 The model below is given as an example of how relative risk levels could be used in determining the appropriate risk mitigation measures:

- From green to any colour: No restrictions or requirements.
- From orange to any colour: Could require passenger locator forms and/or tests, but no travel restrictions.
- From red or grey to any colour (particularly to green): Could restrict traveller's movements depending on symptoms and exposure and/or test.

4.2.5.2 States should consider the following exemptions: crew members, personnel critical for health care delivery and workers essential to maintaining the safety of the airspace should not be made to quarantine unless they are ill or have been in close contact with symptomatic passengers.

Note.— Travellers originating outside of the departure State may need to be separately evaluated upon arrival in comparison to people who were in the departure State for over 14 days. Where a suitable legal and administrative framework is in place to allow for such use, Passenger Name Record (PNR) data, Advance Passenger Information (API), border control records and other passenger information tools could be used to assist in identification of some passengers who do not self-declare.

4.3 SAMPLE SCENARIOS

The case scenarios below are provided as practical illustrations of the risk assessment process outlined above.

Scenario 1

State A has a 7-day rolling average of 7.0 cases per 100 000, a downward trajectory of cases, readily available testing, less than 5 per cent positive tests, and over 25 per cent of hospital beds empty. State B has a 7-day rolling average of 7.8 cases per 100 000, a stable trajectory of cases, readily available testing, less than 2 per cent positive tests, and over 20 per cent availability of hospital beds. States A and B could reasonably enter into a discussion to allow free travel between regions and implement minimal risk mitigation measures.

Options:

- As they are both in the “green” category, no intervention is a potential option.
- Providing passenger information on routine public health measures with public health authority contact details, and requiring reporting should someone become ill.
- Electronic-based monitoring for a period of time if a more active approach is desired.

Scenario 2

State C has a 7-day rolling average of 43.4 cases per 100 000, an increasing disease trajectory, testing only for symptomatic cases and close contacts, over 20 per cent positive tests, and less than 10 per cent available hospital beds. State D has a 7-day rolling average of 12.6 per 100 000, readily available tests, and 20 per cent availability of hospital beds. States C and D could negotiate a risk mitigation agreement where citizens of State D could freely travel to State C, but citizens of State C would be subject to enhanced mitigation strategies.

Options:

- Travellers from State D could move freely about State C with a combination of one or all of the following: traveller education on routine public health measures with public health authority contacts and reporting procedures, electronic based monitoring, and/or traveller questionnaires with contact details.
- Travellers from State C to D could be quarantined with testing for early release, utilize serial testing, or some other active monitoring (smartphone applications, routine call-ins from public health authorities, limited restrictions such as business activities only). Passenger education could be a part of the overarching measures as above. PHC questionnaires could be utilized for rapid contact tracing if necessary.

Scenario 3

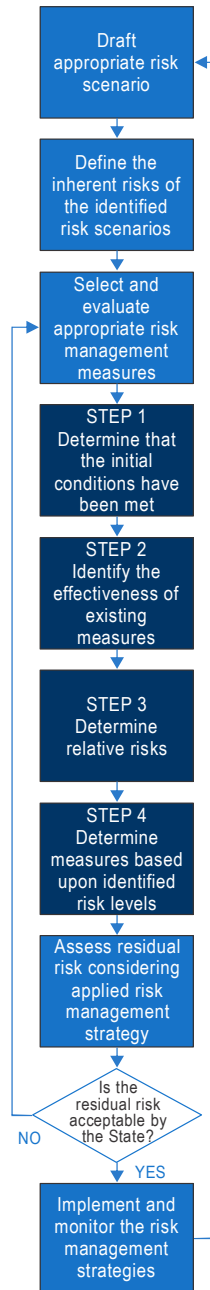
Testing details and hospital data are unavailable. State E has a 7-day rolling average of 30.2 per 100 000 and readily available tests. State F has a 7-day rolling average of 23.6 per 100 000 and tests only available for symptomatic cases and close contacts. State F is dependent on tourism.

Options:

- These States could enter an agreement where persons from State F could travel to State E with minimal mitigation strategies similar to travellers from State D to C as above.
 - Those from State E to F could have slightly enhanced strategies depending on each State's risk tolerance. Options could include some or all of the following: serial testing with reduced or no quarantine, short periods of isolation with a negative test for release, electronic contact tracing/monitoring with daily reporting of symptoms and a post-arrival test at 5-7 days, and/or the use of "do not board" lists for recalcitrant individuals. Passenger education with public health measures and reporting requirements would be critical.
-

Attachment A

DECISION AID



- Draft scenarios to be assessed, considering if the risk is related to passengers, crew members, staff at airports and any other person inside the Public Health Corridor (PHC)
Example: An infectious person, whose condition is unknown or revealed, is boarding an international flight.

- Assess the likelihood of the risk scenario, considering existing management strategies
- Assess the impacts of the risk scenario and its context (health care system, operational, social, political, organizational), considering existing management strategies
- Collect data and information to support qualitative and quantitative assessments
- Define the inherent risk as the combination of the likelihood and impacts of the risk scenario before any actions by the State
Example: The likelihood of an infectious passenger, whose condition is unknown or revealed, to board an international flight, is high. The application of the mitigation measures may result in a reduction of this likelihood.
A probabilistic estimation for the inflight transmission can be defined (x).

States should consider one or more risk management strategies to modify the inherent risk: **Avoidance, Transfer, Mitigation, and Acceptance.**
More information about risk management can be found in Chapter 2 of this manual.
A State may determine that the inherent risk is acceptable depending on its public health capabilities. As needed, the State may select additional mitigation, considering the individual effectiveness and result of combined strategies for risk management.
The mitigation measures for public health risks are described in Chapter 3 of this manual.
In order to select other mitigation measures, useful questions may be posed by the State to help the evaluation of the risk management strategy:

- What is the individual efficacy and effectiveness of each risk mitigation?
- If a risk management strategy is applied, would it reduce the likelihood of an infectious person to contaminate others or reduce the impacts from this contamination in the public health system?
- What are the measures commonly practiced internationally?
- What are the methods available to apply each risk mitigation?
- What would be the recommended procedures to assure or enhance the effectiveness of each risk mitigation?
- To which extent procedures applied in aviation would be applicable to domestic phases of the travel and connection with other modes of transportation?
- Are the risk management strategies coordinated with other national, regional and international stakeholders and the aviation community?

More information about the selection of a combined strategy for risk mitigation is presented in Chapter 4 of this manual.
Example: The States coordinate procedures to be conducted before people engage in air travel, during the flight, in the airport environment and after arrival.
A probabilistic estimation for the transmission at the arrival can be defined (y).

- After the application of the risk management strategy, assess if States are expected to effectively modify the inherent risk
- The residual risk should be evaluated in order to be commensurate with the State's public health capabilities and resilience
Example: After the assessment of combined strategies, the State considers that the residual risk is acceptable.
A probabilistic estimation for the local transmission at the State can be defined (z).

- The State should coordinate actions with other States in order to facilitate air travel
- After the strategies are implemented, their actual effectiveness, efficacy and the stabilization of the residual risk should be continuously monitored
- As States are subjected to changing conditions, it is important to recognize the need to review the risk scenarios and applied mitigation strategies to ensure continuity of traffic connections between States
Example: States should establish indicators and monitor the changing environment of their public health systems and measures implemented by other States in order to identify the need to reassess their initial risk scenario.

Attachment B

EPIDEMIOLOGIC PRIMER

GOAL: Provide the best testing advice to minimize the risk that a person infectious with SARS-CoV-2 could transmit the virus during travel and propose a testing regimen to minimize quarantine.

TERMINOLOGY:

		Disease status		
		Present	Absent	
Screening test result	+	A	B	Total positive tests
	-	C	D	Total negative tests
		Total infected (Ti)	Total not infected (Tni)	Total population (Tp)

A: True Positives
B: False Positives
C: False Negatives
D: True Negatives

Prevalence. Disease burden, expressed as a percentage or rate with the total population as the denominator. Prevalence in this context refers to the number of existing cases of disease in a specified population at a given point in time.

Incidence. Number of new cases of disease in a specified population during a specified period of time.

Sensitivity. The likelihood that a test will correctly identify a person with the disease. $A/(A+C)$ is the mathematical formula.

Specificity. The likelihood that a test will correctly identify a person without the disease. $D/(B+D)$ is the mathematical formula.

Positive predictive value (PPV). How likely a positive test is a true positive. $A/(A+B)$ is the mathematical formula.

Negative predictive value (NPV). How likely a negative test is true negative. $D/(C+D)$ is the mathematical formula.

STEP ONE

Determine test performance requirements to maximize the number of people who could travel with reasonable certainty.

Prevalence assumptions/issues

1. It is important to know who might be infectious during travel as opposed to prevalence since the beginning of the outbreak. This is calculated by multiplying the incidence with the time period of infectiousness.
2. The Brown School of Public Health website is one of the best sites tracking the incidence or current new cases per 100 000 people: <https://globalepidemics.org/key-metrics-for-covid-suppression/>. However, it should be noted that some statistics might not be accurate due to limitations of testing and reporting systems.
3. Among those who are sick, the vast majority of people are infectious from two days prior to symptom onset to nine days following symptom onset; hence, 12 days are used to determine the time period where people could infect others.
4. The asymptomatic rate is assumed to be 40 per cent in accordance with a CDC reference published in July: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html>. This implies that 60 per cent of people are symptomatic. Further assuming that mainly symptomatic people get tested, the number of positive tests represents only 60 per cent of the total number of people who are potentially infectious.

Calculating prevalence

To calculate the prevalence of potentially infectious people with positive tests, use the Brown daily average of new cases per 100 000 people (a 7-day moving average; based on Assumption 2 above) and multiply it by 12 (the number of days a person might be infectious; based on Assumption 3 above).

$$\begin{aligned}\text{Prevalence} &= \text{incidence} \times \text{duration} \\ &= \text{number of people per 100 000 with positive tests} \times 12 \\ &= \text{potentially infectious people with positive tests per 100 000 people}\end{aligned}$$

Taking into account that the number of positive tests represents only 60 per cent of the total number of people who are potentially infectious, the total number of potentially infectious people needs to be calculated. Setting the total number of people who might be potentially infectious as "X", the number of people with positive tests must equal 0.6 times "X" (based on Assumption 3 above).

$$\begin{aligned}\text{Potentially infectious people with positive tests} &= 0.6 \times \text{total number of potentially infectious people ("X")}; \\ \text{Total number of potentially infectious people ("X")} &= \text{Potentially infectious people with positive tests} / 0.6\end{aligned}$$

To calculate the prevalence percentage, divide "X" by 100 000 to get the ratio, then multiply it by 100 to get the percentage.

$$\begin{aligned}\text{Prevalence percentage} &= \text{ratio} \times 100 \\ &= \text{"X"} / 100\,000 \times 100 \\ &= x \text{ per cent}\end{aligned}$$

Example:

For State A, using the data from 21 September 2020 with a daily average of 12.6 per 100 000 people, the equations are as follows:

$$\begin{aligned}
 \text{Prevalence} &= \text{incidence} \times \text{duration} \\
 &= \text{number of people per 100 000 with positive tests} \times 12 \\
 &= 12.6 \text{ per 100 000} \times 12 \\
 &= 151.2 \text{ potentially infectious people with positive tests per 100 000 people}
 \end{aligned}$$

$$\text{Potentially infectious people with positive tests} = 0.6 \times \text{total number of potentially infectious people}$$

$$\begin{aligned}
 \text{Total number of potentially infectious people (X)} &= \text{Potentially infectious people with positive tests} / 0.6 \\
 &= 151.2 \text{ per 100 000} / 0.6 \\
 &= 252 \text{ per 100 000 people}
 \end{aligned}$$

$$\begin{aligned}
 \text{Ratio} &= X / 100\,000 \\
 &= 252 / 100\,000 \\
 &= 0.00252
 \end{aligned}$$

$$\begin{aligned}
 \text{Prevalence percentage} &= 0.00252 \times 100 \\
 &= 0.252 \text{ per cent}
 \end{aligned}$$

Quick calculation of prevalence:

Because the only variable in this calculation that changes is the daily average, while all others are fixed, the whole calculation can be done by simply dividing the daily average per 100 000 people by 50. For example, State A with a daily average of new cases per 100 000 people of 12.6 has a prevalence of $12.6 / 50 = 0.252$ per cent. It should be noted that this is only valid if the number of new cases is expressed per 100 000 people.

Performing the same functions for State B (7-day rolling average of 14.6/100 000) and State C (24.6/100 000 and the highest average on the Brown site) yields 0.292 and 0.492 per cent.

Performing 2 x 2 tables

- The tables were developed initially with the sensitivity and specificity of the most recent Emergency Use Agreement applications to the United States Food and Drug Administration (FDA) for the Abbot Rapid test (sensitivity of 97.1 per cent and specificity of 98.5 per cent).
- Then, the same prevalence values were run with the worst listed sensitivity (80 per cent) and specificity (92 per cent) on the John Hopkins' compendium of all COVID-19 tests currently approved.
- For additional comparison, the values for the poorest performing test were run using the highest prevalence in the United States County X.
- Finally, the tables were populated using the proposed sensitivity and specificity of 95 per cent.
- PCR testing typically has higher sensitivities and specificities and would have even higher performance.

Calculations used for the 2 x 2 tables

A quick reminder of the 2 x 2 table terminology:

T_p = the total number of people in the population

P = the prevalence as calculated above (daily average of new cases per 100 000 people divided by 50)

T_i = the total number of infected people in the population

T_{ni} = the total number of people in the population who are not infected

A = the total number of people who are true positive

B = the total number of people who are false positive

C = the total number of people who are false negative

D = the total number of people who are true negative

The calculations are as follows:

P = daily average of new cases per 100 000 people / 50

$T_i = A + C = T_p \times P$

$T_{ni} = B + D = T_p - T_i$

Sensitivity = $A / (A + C)$

Specificity = $D / (B + D)$

PPV = $A / (A + B)$

NPV = $D / (C + D)$

(Prevalence of 10 per cent, sensitivity of 95 per cent, specificity of 95 per cent)

Step 1 — Using a population of 1 000, calculate the disease burden.

		Disease status		
		Present	Absent	
Screening test result	+			1 000 x 0.10 = 100 with the disease 1 000 - 100 = 900 without the disease
	-			
		100	900	1 000

Step 2 — Using sensitivity, calculate A (true +) and C (false -).

		Disease status		
		Present	Absent	
Screening test result	+	95		100 x 0.95 = 95 true positives
	-	5		100 - 95 = 5 false negatives
		100	900	1 000

Step 3 — Using specificity, calculate B (false +) and D (true -). Then, add up test positives and negatives.

		Disease status		
		Present	Absent	
Screening test result	+	95	45	140
	-	5	855	860
		100	900	1 000

900 x 0.95 = 855 true negatives
900 - 855 = 45 false positives

Step 4 — Calculate the positive predictive value (PPV) and the negative predictive value (NPV).

$$\text{PPV} = \text{true positives/test positives} = (95/140) \times 100 = 67.8 \text{ per cent}$$

$$\text{NPV} = \text{true negatives/all negatives} = (855/860) \times 100 = 99.4 \text{ per cent}$$

Examples of calculations

(Varying prevalence, sensitivity and specificity)

Example 1

State A: Prevalence of 0.25 per cent, Abbott Emergency Use Authorized with a sensitivity of 97.1 per cent and a specificity of 98.5 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	2 428	14 962	17 390
	-	72	982 538	982 610
		2 500	997 500	1 000 000

$$\text{PPV} = (2\,428/17\,390) \times 100 = 14.0 \text{ per cent}$$

$$\text{NPV} = (982\,538/982\,538) \times 100 = 99.99 \text{ per cent}$$

Example 2

State B: Prevalence of 0.292 per cent, Abbott Emergency Use Authorized with a sensitivity of 97.1 per cent and a specificity of 98.5 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	2 835	14 956	17 791
	-	85	982 124	982 209
		2 920	997 080	1 000 000

$$PPV = (2\,835/17\,791) \times 100 = 15.9 \text{ per cent}$$

$$NPV = (982\,124/982\,209) \times 100 = 99.99 \text{ per cent}$$

Example 3

State C: Prevalence of 0.492 per cent, Abbott Emergency Use Authorized with a sensitivity of 97.1 per cent and a specificity of 98.5 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	4 777	14 926	19 703
	-	143	982 154	980 297
		4 920	995 080	1 000 000

$$PPV = (4\,777/19\,703) \times 100 = 24.2 \text{ per cent}$$

$$NPV = (980\,154/980\,297) \times 100 = 99.98 \text{ per cent}$$

Example 4

State A: Prevalence of 0.25 per cent, worst case test with a sensitivity of 80 per cent and a specificity of 92 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	2 000	79 800	81 800
	-	500	917 700	918 200
		2 500	997 500	1 000 000

$$PPV = (2\,000/81\,800) \times 100 = 2.5 \text{ per cent}$$

$$NPV = (917\,700/918\,200) \times 100 = 99.94 \text{ per cent}$$

Example 5

State B: Prevalence of 0.292 per cent, worst case test with a sensitivity of 80 per cent and a specificity of 92 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	2 336	79 766	82 108
	-	584	917 314	917 898
		2 920	997 080	1 000 000

$$PPV = (2\,336/82\,108) \times 100 = 2.8 \text{ per cent}$$

$$NPV = (917\,314/917\,898) \times 100 = 99.93 \text{ per cent}$$

Example 6

State C: Prevalence of 0.492 per cent, worst case test with a sensitivity of 80 per cent and a specificity of 92 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	3 936	79 606	83 542
	-	984	915 474	916 458
		4 920	995 080	1 000 000

$$PPV = (3\,936/83\,542) \times 100 = 4.7 \text{ per cent}$$

$$NPV = (915\,474/916\,458) \times 100 = 99.89 \text{ per cent}$$

Example 7

County X: Prevalence of 5.994 per cent, worst case test with a sensitivity of 80 per cent and a specificity of 92 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	47 952	75 208	123 157
	-	11 988	864 855	876 843
		59 940	940 060	1 000 000

$$PPV = (47\,952/123\,157) \times 100 = 38.9 \text{ per cent}$$

$$NPV = (864\,855/876\,843) \times 100 = 98.6 \text{ per cent}$$

Example 8

State A: Prevalence of 0.25 per cent, worst case test with a sensitivity of 95 per cent and a specificity of 95 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	2 375	50 000	52 375
	-	125	947 625	947 750
		2 500	997 500	1 000 000

PPV = $(2\,375/52\,375) \times 100 = 4.75$ per cent, or only 1 out of approximately 20 will be a true positive.

NPV = $(947\,625/947\,750) \times 100 = 99.99$ per cent, or 1 in approximately 10 000 testing negative might be positive.

Example 9

State B: Prevalence of 0.292 per cent, worst case test with a sensitivity of 95 per cent and a specificity of 95 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	2 774	49 854	52 628
	-	146	947 226	947 372
		2 920	997 080	1 000 000

PPV = $(2\,774/52\,628) \times 100 = 5.27$ per cent, or only 1 out of approximately 20 will be a true positive.

NPV = $(947\,226/947\,372) \times 100 = 99.98$ per cent, or 1 in approximately 10 000 testing negative might be positive.

Example 10

State C: Prevalence of 0.492 per cent, worst case test with a sensitivity of 95 per cent and a specificity of 95 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	4 674	49 754	54 428
	-	246	945 326	945 572
		4 920	995 080	1 000 000

PPV = $(4\,674/54\,428) \times 100 = 8.59$ per cent, or nearly 1 out of 10 will be a true positive.

NPV = $(945\,326/945\,572) \times 100 = 99.97$ per cent, or 1 in approximately 5 000 testing negative might be positive.

Example 11

County X: Prevalence of 5.994 per cent, worst case test with a sensitivity of 95 per cent and a specificity of 95 per cent.

		Disease status		
		Present	Absent	
Screening test result	+	56 943	48 003	103 946
	-	2 997	893 057	896 054
		59 940	940 060	1 000 000

PPV = (56 943/103 946) x 100 = 54.78 per cent, or slightly over 1 out of 2 will be a true positive.

NPV = (893 057/896 054) x 100 = 99.67 per cent, or 1 in approximately 300 with a negative test might be positive.

Notes:

- 1.— The prevalence does not affect the performance of the test with respect to the sensitivity and specificity. It affects the number of infected and uninfected persons in a cohort of people.
- 2.— As prevalence goes up when performing a screening test, so does the positive predictive value.
- 3.— In a low prevalence situation, the negative predictive value is very little affected by even relatively poor performing tests.
- 4.— Poor performing tests will significantly increase the number of false positives who would be denied boarding, at least initially until confirmatory test can be completed.

Justifications for setting the minimum sensitivity and specificity levels at 95 per cent

1. It will allow a wider range of test devices to be used that are currently fielded as opposed to forcing States to procure newer models that are frequently hard to obtain.
2. The wider range also allows for the use of rapid antigen tests as a screening device which are more accessible and practical for application in the aviation environment; which are much faster and less expensive to use. In addition, it would reserve the more expensive real-time RT-PCR tests for confirmation of positives in conjunction with clinical correlation.
3. Setting the specificity at 95 per cent maintains a high NPV and reduces the false positives.
4. Setting the sensitivity at 95 per cent will reduce the risk of false negatives and improve the PPV.
5. In low prevalence settings (equating to 10-25 cases per 100 000 on a rolling average), the NPV equates to mislabelling an infected person as negative between 1 in 5 000 and 10 000 negative tests. In higher prevalence settings (equating to over 50 cases per 100 000 on a rolling average), the mislabelling rises close to 1 in 300.
6. In the same low prevalence and higher prevalence range, the PPV improves from correctly labelling a positive from approximately 1 in 10 to 20, to slightly better than 1 out of 2 of positive tests.
7. Few States set their sensitivity and specificity higher leading to further improvements in test performance.

STEP TWO: Pre-departure testing interval**Assumptions**

- Incubation time: 2-12 days (95 per cent) with a median of 5-6 days.
- Shedding can occur 48 hours prior.
- The most sensitive tests turn positive 1-3 days prior to symptoms.
- Leaving a 2- to 4-day period where a person could be infected but not infectious with a negative test.
- The goal is to limit infectivity in flight.

Considerations

1. If the testing is placed at 72 hours before their departure, at least 60 per cent of those infected with a negative test will manifest their illness and hopefully remove themselves from travel even if they were infected walking into the testing facility.
2. If the person with a negative test is a true negative and becomes infected walking out of the testing facility, they should not begin shedding the virus in most cases until after arrival at the destination.
3. Moving testing to 48 hours prior to departure would potentially let a few more of the negative but infected slip through who could begin shedding the virus in flight before developing symptoms, but would increase the likelihood that a person subsequently infected would not become infectious in flight.

STEP THREE: Can quarantine be reduced with serial testing?**Considerations**

Consideration was given to two studies from the United Kingdom examining the relative effectiveness of various health measures on arrival to reduce the potential for onward transmission. It is summarized below:

- Quarantine of 14 days (Gold Standard): 78-99 per cent effective
- Single RT-PCR upon arrival: 39.6 per cent effective (2 in 5 cases detected)
- Single RT-PCR at 4 days after arrival: 64.3 per cent effective
- Single RT-PCR at 5 days after arrival: 88 per cent effective
- Upon arrival and 4 days after arrival (two tests): 68.9 per cent effective
- Single RT-PCR at 7 days after arrival: 94 per cent effective

Discussion

1. Assuming the effective percentages are the ability to find the people who could transmit the disease after release from quarantine, it seems reasonable to say that a 5 or 7-day window prevents most of the subsequent transmigration of disease.
2. The question is whether testing 72 hours prior to arrival, with a second test on day 4 or 5, would approach the 94 per cent effectiveness described for a single TR-PCR test 7 days after arrival.
3. Logically, it would appear a 7-day window of proven negativity would provide the same level of effectiveness.

Notes for consideration

- 1.— *In the screening environment, the exact test is not as important as the technique in conjunction with the sensitivity and specificity. The sensitivity and specificity should be of at least 95 per cent and performed by people adequately trained using the techniques specified by the manufacturer. Laboratory certification is preferred.*
- 2.— *Evaluation of the positive cases must be considered.*
- 3.— *With the level of prevalence in various States, the PPV with the best tests available are going to be in the 10 to 25 per cent range, meaning 1 in 4 to 10 will be true positives.*
- 4.— *The other 75 to 90 per cent will be false positives and denied boarding.*
- 5.— *If less sensitive and specific tests are used for screening, the numbers go up significantly to as many 24 out of 25 positive tests being false positives.*
- 6.— *Furthermore, some of the true positives may be shedding viral remnants and no longer be infectious and could therefore travel.*
- 7.— *Clinical correlation and more definitive testing will be required in case of positive screening test results.*
- 8.— *States should consider what form would be acceptable to declare someone with a positive test as not infectious and ready to travel.*

— END —

ISBN 978-92-9265-220-3



9

789292

652203